P29 SINGAPORE CHILDHOOD CANCER SURVIVOR STUDY – A MULTI-INSTITUTIONAL COLLABORATIVE STUDY ON LONG-TERM SURVIVORS OF CHILDHOOD CANCER

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Background: Worldwide, survival rates among childhood cancer patients are increasing; thus, assessing the risk of late effects and complications is important.

Methods: The Singapore Childhood Cancer Registry (1981–2005) included 704 patients from KK Women's and Children's Hospital and 626 from the National University Hospital (NUH). The Singapore Childhood Cancer Survivor Study (SIN-CCSS) consisted of all individuals who survived at least 2 or more years after treatment for cancer diagnosed during childhood or adolescence.

Findings: A total of 1043 (72.4%) of 1440 patients are alive, of which 839 (80.4%) are long-term survivors. 58.6% ($n = 492$) survivors had haematological malignancies, whereas 41.4% ($n = 347$) were diagnosed with various solid tumours. To date, 79 survivors have enrolled in the study at NUH. Mean age was 14.9 years (range 4.9–31.8); 55.7% were male, 11.4% were an only child, 58.2% were Singaporean, and 74.4% were Chinese. 27.8% continued to see the doctor once or twice per year and 12.7% of these visits were related to previous illness. Preliminary analysis shows that 21.8% of participants reported anxiety. Endocrine adverse effects were most common (40.4%), followed by respiratory complaints (37.9%).

Interpretation: At least 58% of those diagnosed with childhood cancer are long-term survivors. This is the first study of its kind in Singapore, looking at long-term survivors of childhood cancer with a multicultural and multiethnic approach. In the future, we plan to focus on prevention of late effects, aetiological (genetic and environmental) and outcomes research, and survivor education.

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P30 MICRORNA AS DIAGNOSTIC AND PROGNOSTIC MARKERS IN HUMAN HEPATOCELLULAR CARCINOMAS

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Background: Human hepatocellular carcinomas (HCCs) are the fifth most common malignant tumours worldwide, and the third leading cause of cancer-related death. In view of the high postoperative recurrence rate, identification of potential biomarkers should be considered; these can be a diagnostic marker, prognostic marker, or target for cancer therapy. MicroRNAs (miRNAs) have been proposed to contribute to oncogenesis because they can function either as tumour suppressors or oncogenes.

Methods To search the useful index marker to predict postoperative recurrence rate of patients with HCC, adjacent noncancerous liver tissues from HCC patients with good prognosis ($n = 6$) and poor prognosis ($n = 6$) were collected. 270 miRNA expression profiles were analysed using a highly sensitive stem-loop reverse transcriptase (RT)-PCR method.

Findings: 20 miRNA candidates were found that were association with good and poor prognosis. Further screening of 216 adjacent non-cancerous liver tissues identified six miRNAs significantly correlated with disease-free survival ($p < 0.021$). Cox proportional-hazards analysis revealed that high expression of miR-A6 and miR-A18 were the most significant markers associated with poor disease-free survival ($p = 0.013$, hazard ratio [HR] 1.633 [95% CI 1.108–2.408]; $p = 0.001$, HR 1.929 [1.298–2.867], respectively). High expression of miR-A3 and miR-A19 were the most significant markers related to better disease-free survival ($p = 0.012$, HR 0.431, 95% CI [0.224–0.830]; $p = 0.001$, HR 0.529, [0.357–0.783], respectively). Additionally, in J7 cells transduced with anti-miR-A6 lentivirus, cell-growth suppression was observed and cell-cycle related molecules, including CDK2, CDK4, cyclin E, and cyclin D1, were underexpressed.

Interpretation: miRNAs associated with good and bad prognosis can serve as biomarkers for HCC.

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P31 EXPRESSION OF NEUROENDOCRINE MARKERS IN NON-SMALL-CELL LUNG CARCINOMAS AND ASSOCIATION WITH POST-OPERATIVE SURVIVAL

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Introduction: Neuroendocrine differentiation has been suggested as a marker of poor prognosis in 10–30% of non-small-cell lung carcinomas (NSCLCs). We studied immunohistochemical expression of the neuroendocrine markers chromogranin A (CgA), synaptophysin (SYN), histidine decarboxylase (HDC), and neuron-specific enolase (NSE) in various subtypes of NSCLCs, and noted whether there was any association with post-operative survival.

Methods: 225 patients (mean age 45 years) diagnosed with NSCLCs were surgically treated at Gulab Devi Chest Hospital, Lahore, Pakistan from January, 2004, to January, 2006. Relevant clinical and laboratory data including age, sex, tumour location, and type of surgical procedure were recorded in separate proformas. After haematoxylin and eosin staining, paraffin-embedded tissue blocks of tumour specimens were stained immunohistochemically with monoclonal anti-CgA, anti-SYN, anti-HDC, and anti-NSE antibodies. A total of 153 patients were followed up for 4.5 years, and the shortest follow-up time was 13 months. COX proportional-hazard multivariate analysis was applied to observe

the relationship between the NSCLC neuroendocrine markers and post-operative survival.

Findings: The subtypes of NSCLCs included in the study were 54% squamous-cell carcinomas (SCCs), 32.5% adenocarcinomas, and 11.5% large-cell lung carcinomas (LCLCs). 10.2%, 17.3%, 15.1%, and 7.4% of NSCLC tissue demonstrated focal to almost diffuse strong cytoplasmic staining of the tumour cells with CgA, SYN, HDC, and NSE, respectively. Assessing individual subtypes showed that 3.8%, 5.1%, 6.5%, and 1.8% SCCs, 13.3%, 17.3%, 20%, and 9% adenocarcinomas, and 21.3%, 28%, 33%, and 16.6% LCLCs demonstrated positive staining with CgA, SYN, HDC, and NSE, respectively. HDC expression was stronger and more sensitive than CgA, SYN, and NSE ($p = 0.0063$). Multivariate analysis showed that the NSCLC patients with neuroendocrine markers had significantly shorter survival ($p = 0.031$). The following factors were related to survival: lung-cancer histological differentiation ($p = 0.0057$), clinical stage ($p = 0.001$), and neuroendocrine markers reaction ($p = 0.072$).

Interpretation: Neuroendocrine markers in NSCLC are significantly associated with cancer-cell differentiation and post-operative survival. These markers should be applied clinically as prognostic factors for post-operative survival of NSCLC patients.

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P32 EXPRESSION OF BCL-2 ONCOPROTEIN IN WOMEN OF REPRODUCTIVE AGE WITH UTERINE SMOOTH-MUSCLE TUMOURS IN PAKISTAN

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Background: BCL-2 oncoprotein has an important role in cell development, maturation, and replication by reducing the requirement for growth factors, and acts as an anti-apoptotic factor in various neoplastic processes. This study investigated immunohistochemical expression of BCL-2 protein in uterine leiomyomas, smooth-muscle tumours of uncertain malignant potential (STUMP), and leiomyosarcomas (LMS), in female patients of child-bearing age. The correlation between BCL-2 expression and various clinicopathological parameters was assessed to evaluate its prognostic value.

Methods: A total of 66 female patients (mean age 37 years, SD 4.5) presenting with uterine leiomyomas ($n = 42$), STUMP ($n = 18$), and LMS ($n = 6$) from July, 2005, to July, 2006, at the departments of Gynecology and Obstetrics in tertiary-care hospitals in Lahore, Pakistan, were included. Paraffin-embedded tissues of these patients were subjected to BCL-2 immunohistochemistry. Findings were compared and correlated with different clinicopathological parameters. Clinical information, including follow-up data until July, 2010, was obtained from the database of the hospitals.

Findings: Positive BCL-2 immunostaining was observed in two of six patients with LMS, 11 of 18 with STUMP, and 39 of 42 with leiomyomas. Frequency of BCL-2 expression and staining intensity were significantly different between LMS and leiomyoma ($p < 0.05$), as well as STUMP and leiomyoma ($p < 0.05$), but not between LMS and STUMP ($p > 0.05$). No significant association was found between BCL-2 immunostaining and tumour size, age, menstrual history, parity, infertility, contraceptive measures, or family history of neoplasms. Patients with uterine LMS who had BCL-2 positive tumours showed less vascular-space involvement and longer overall survival than patients with BCL-2 negative tumours ($p < 0.05$).

Interpretation: Expression of BCL-2 oncoprotein is more frequent and strong in leiomyomas than in LMS and STUMP. Stronger BCL-2 expression in benign leiomyomas and the better clinical outcome of BCL-2-positive LMS indicate that this protein is a good prognostic factor. Larger studies are needed to establish BCL-2 as a routine marker for improved prognosis in malignant uterine smooth-muscle tumours.

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P33 PREDICTION OF PATHOLOGICAL GRADE OF ASTROCYTOMAS USING MRI – A NEW METHOD VERSUS CLINICIAN PERFORMANCE

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Background: Astrocytoma is the most common glioma and has poor prognosis, affected by treatment strategy and pathological grading. Pre-operative assessment of grades is difficult. The aim of this study was to evaluate a support vector machine (SVM) model to help clinicians predict grading of astrocytomas.

Methods: 106 patients were recruited at our hospital between January, 2008, and April, 2009. Two clinicians read MRIs and scored the appearance of astrocytomas, and a support vector machine (SVM) model was constructed. From clinicians' predictions, predictions of the SVM model, and predictions of clinicians with the SVM model, three receiver operating characteristic (ROC) curves were created to discriminate low-grade and high-grade groups.

Findings: The area under the curve (AUC) for clinicians' predictions was 0.7881, which was significantly less than the AUC for the SVM model (0.9370, χ^2 8.62, $p = 0.0033$) and the AUC for clinicians with the SVM model (0.8829, χ^2 13.46, $p = 0.0002$). However, the AUCs of the SVM model and clinicians with the SVM model did not differ significantly (χ^2 1.63, $p = 0.2011$).

Interpretation: The SVM model is a useful mathematical method that can help clinicians improve the accuracy of predicting pathological grade of astrocytomas.

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